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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/558,626	11/29/2005	Christopher David Beadle	X-15735	3887

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EXAMINER	
HOLT, ANDRIAE M	

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
11/03/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

Office Action Summary	Application No.	Applicant(s)	
	10/558,626	BEADLE ET AL.	
	Examiner	Art Unit	
	Andriae M. Holt	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,10,11,13,14,16,17,19,24 and 29* is/are pending in the application.

4a) Of the above claim(s) *10,11,13,14,16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,19,24 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/29/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4, 10-11, 13-14, 16-17, 19, 24, and 29 are pending in the application. The examiner acknowledges the preliminary amendment filed on November 29, 2005, in which claims 5-9, 12, 15, 18, 20-23, 25-28 and 30-36 were cancelled.

Election/Restrictions

The examiner inadvertently restricted the wrong set of claims. The examiner has considered applicant's request to withdraw the restriction requirement in view of the preliminary amendment filed November 29, 2005. The Election/Restriction requirement set forth in the Office Action dated May 2, 2008 is hereby withdrawn.

The examiner acknowledges the election of species example 38, N-propyl-N-{[2-(trifluoromethyl) phenyl] methyl}-pyrrolidin-3-amine **with** traverse. The traversal is on the grounds that the restriction requirement is improper according to PCT rules and that Ar_1 is limited to phenyl. The examiner acknowledges that the improper restriction requirement in view of the preliminary amendment filed November 29, 2005. However, formula (I), even with the limitation that Ar_1 is phenyl, still encompasses a vast number of compounds as R^1 can be n-propyl, 1-methylethyl, 2-methylpropyl or 3, 3-dimethylpropyl, $(CH_2)_q$-Ar_2 or a group of formula (i) or (ii). Each of which represent a wide variety of compounds with different properties and that would require a different search of the art. The election will be used for search purposes to advance prosecution.

Claims 10-11, 13-14 and 16-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no

allowable generic or linking claim. Election was made **with** traverse in the reply filed on July 2, 2008.

The election of species is made final.

Claims 1-4, 19, 24, and 29 will be examined on the merits.

Priority

The application is a 371 of PCT/US04/13004 filed on May 11, 2004, which claims benefit to US Provisional Applications 60/510,867 filed October 14, 2003, 60/524,450 filed November 24, 2003 and 60/524,781 filed November 25, 2003. Priority to United Kingdom Foreign Application No. 0313463.2 filed June 11, 2003 is acknowledged.

Information Disclosure Statement

Receipt of Information Disclosure Statements filed on November 29, 2005 is acknowledged.

Initially, the Examiner searched for Applicant's elected species, N-propyl-N-{[2-(trifluoromethyl) phenyl] methyl}-pyrrolidin-3-amine. However, since no prior art was found which could be used to reject the claims, the search was expanded to encompass the broader claim 1. The search was not further expanded because prior art was found to reject compounds embodied by formula (I).

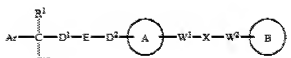
The examiner notes that US 6,906,072 is being used as the English equivalent for WO 01/53258 for translation purposes.

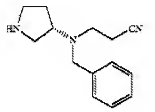
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 19, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Yamamoto et al. (WO 01/53258).

Yamamoto et al. disclose a novel nitrogen-containing compound which is represented by formula (I)  (Abstract, translation). Yamamoto et al. teach that ring A indicates any one ring selected from pyrrolidine ring (col. 18, lines 58-61). Yamamoto et al. disclose in col. 155, example 175, the synthesis of (3S)-3-[N-2-cyanoethyl)-N-benzylamino] pyrrolidine



. (3S)-3-[N-2-cyanoethyl)-N-benzylamino] pyrrolidine anticipates compounds of formula (I), wherein, Ar_1 is phenyl and $R^1$is selected from –CN. (3S)-3-[N-2-cyanoethyl)-N-benzylamino] pyrrolidine also anticipates 3-[(phenylmethyl)-(3S)-3-pyrrolidinylamino]-propanenitrile, as it is the same compound. Yamamoto et al. disclose (3S)-3-[N-2-cyanoethyl)-N-benzylamino] pyrrolidine is combined with iodide C. Iodide can function as an antioxidant as it is a reducing species. Yamamoto et al. disclose the compounds can be formulated into tablets, powders, granules, syrups, and the like (col. 27, lines 21-27, translation). Yamamoto et al. disclose excipients, binders, disintegrants, lubricants and antioxidants can be used for formulation preparations (col. 27, lines 27-35, translation) (pharmaceutical preparation, instant invention). Yamamoto et al. disclose the compounds represented by formula (I), a salt thereof or a hydrate is useful as a calcium antagonist and specifically, a neuron-selective calcium antagonist (col. 28, lines 63-67).

Yamamoto et al. do not specifically teach that (3S)-3-[N-2-cyanoethyl)-N-benzylamino] pyrrolidine can be used as a method of treating attention-deficit hyperactivity disorder by selectively inhibiting the reuptake of norepinephrine over serotonin and dopamine, however, (3S)-3-[N-2-cyanoethyl)-N-benzylamino] pyrrolidine is a compound that falls within the bounds of compounds of formula (I) and recited in claim 24 of the instant application. Therefore, it is duly noted that the compound of the

prior art is the same as Applicant's compound. Thus, the skilled artisan would recognize that a compound is inseparable from its properties. Hence, all the properties associated with Applicant's compound would also be possessed by the compound of the prior art.

Yamamoto et al. meet all of the limitations of the claims and the claims are thereby anticipated.

Claim Rejections - 35 USC § 103

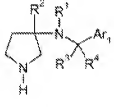
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 29 is rejected under 35 U.S.C. 103 (a) as being unpatentable over Yamamoto et al. (WO 01/53258).

Applicant's Invention

Applicant claims a composition comprising a compound of general formula I



(I)

Applicant further claims a method of treating attention-deficit hyperactivity disorder (ADHD) by administering to a patient in need an effective amount of a compound of

claim 1, which selectively inhibits the reuptake of norepinephrine over serotonin and dopamine.

Determination of the scope of the content of the prior art
(MPEP 2141.01)

The teachings of Yamamoto et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed above.

Ascertainment of the difference between the prior art and the claims
(MPEP 2141.02)

Yamamoto et al. do not specifically teach a method of treating attention-deficit hyperactivity disorder.

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of the Yamamota et al. and use the compositions as taught by Yamamoto et al. to treat attention deficit hyperactivity disorder by inhibiting the reuptake of serotonin uptake. One skilled in the art at the time the invention was made would have been motivated to use the compounds as Yamamoto et al. teach the compounds are useful as a neural cell death depressor and an agent for treating neural disease, such as Alzheimer's disease, Parkinson's disease, pain, schizophrenia, migraine, manic-depression, and cerebral disorders, which are the same disorders as taught in Applicant's specification that can be treated with the compounds of formula (I). The disorders are all neurological disorders that can be treated with similar

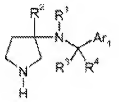
medicaments, thus, it would have been obvious to the skilled artisan that compounds as taught by Yamamoto et al. would be able to useful in treating attention deficit hyperactivity disorder also.

Therefore, the claimed invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because every element of the invention has been fairly suggested by the cited references.

Claim 29 is rejected under 35 U.S.C. 103 (a) as being unpatentable over Yamamoto et al. (WO 01/53258) in view of Hertel et al. (US 6,353,008).

Applicant's Invention

Applicant claims a composition comprising a compound of general formula I



(I)

Applicant further claims a method of treating attention-deficit hyperactivity disorder (ADHD) by administering to a patient in need an effective amount of a compound of claim 1, which selectively inhibits the reuptake of norepinephrine over serotonin and dopamine.

Determination of the scope of the content of the prior art
(MPEP 2141.01)

The teachings of Yamamoto et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed above.

Ascertainment of the difference between the prior art and the claims
(MPEP 2141.02)

Yamamoto et al. do not specifically teach a method of treating attention-deficit hyperactivity disorder. It is for this reason Hertel et al. is joined.

Hertel et al. teach compounds which have selective activity as antagonists and partial agonists of the serotonin-1_A receptor and the serotonin-2_A receptor, and activity as inhibitors of serotonin reuptake (col. 1, lines 38-41). Hertel et al. further teach the invention provides a method of inhibiting the reuptake of serotonin and antagonizing the 5-HT_{1A} receptor which comprises administering to a subject in need of such treatment an effective amount of a compound of formula I (col. 2, lines 63-67). Hertel et al. teach in example 1a, col. 26, the preparation of 1-(t-butoxycarbonyl)-3-(7-benzo (b) thiophene)-3-hydroxy pyrrolidine and several other examples the preparation of pyrrolidine compounds that of inhibiting the reuptake of serotonin. Hertel et al. teach treatment methods are useful for treating many other diseases, disorders and conditions, including attention deficit hyperactivity disorder (col. 72, lines 57-58 and col. 73, line 16).

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of the Yamamota et al. and Hertel et al. and use the compositions as taught by Yamamoto to treat attention deficit hyperactivity disorder by inhibiting the reuptake of serotonin uptake. Hertel et al. teach that pyrrolidine compounds are potent inhibitors of serotonin and provide an increase in the availability of serotonin, norepinephrine and dopamine to provide improved activity in treating disorders such as attention deficit hyperactivity disorder. One skilled in the art at the time the invention was made would have been motivated to use the compounds as taught by Yamamoto et al., as the compounds have the same core structure as the compounds taught by Hertel et al., pyrrolidine which are potent inhibitors of serotonin reuptake. Given the state of the art as evidenced by the teachings of the cited references, and absent any evidence to the contrary, there would have been a reasonable expectation of success in combining the teachings of the cited references to use the compounds to effectively treat attention deficit hyperactivity disorder by the inhibition of serotonin reuptake and increasing the availability of serotonin, norepinephrine and dopamine.

Therefore, the claimed invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because every element of the invention has been fairly suggested by the cited references.

None of the claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is 571-272-9328. The examiner can normally be reached on 7:00 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richter Johann can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Andriae M. Holt
Patent Examiner
Art Unit 1616

/John Pak/
Primary Examiner, Art Unit 1616